REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested.

As an initial matter, Applicants thank Examiner Blessing M. Fubara for her courtesy extended during the interview with Applicants' representatives, Mr. David D. McMasters and Dr. Karen B. Geahigan, on May 29, 2008.

Claims 1, 2, 13-15, 20-54, 65-72, 90-93, 98, 99, 102, 114, 115, 118-147, 158-164, 182-192, 198-203 and 232-237 were pending. Claims 14, 15, 20-26, 90-93, 114, 115, 118-124, 200-203, 236 and 237 have been canceled without prejudice to future prosecution in a related application. Accordingly, claims 1, 2, 13, 27-54, 65-72, 90-93, 98, 99, 102, 125-147, 158-164, 182-192, 198, 199, and 232-235 are pending.

Claims 28-33, 42-54, 65, 66, 70, 71, 98, 99, 102, 125-147, 158-164, 182-192, 198, 199, and 233 are withdrawn from consideration as directed to the non-elected invention or species. Claims 1, 2, 13, 27, 34-41, 67-69, 72 and 232 are under consideration. In addition, claim 234 has been amended to depend on claim 69 (which is under consideration). Thus, claim 234 and its dependent claim, claim 235, are also under consideration in the present application.

Claims 1, 2, 13, 27-54, 65-72, 98, 159, 164, 182, 189, 198, 199 and 232-235 have been amended. The amendments have been made to facilitate allowance and without acquiescing to the rejections in the Office Action or prejudice to future prosecution of the previously pending claims in a related application. Claim 1 has been amended to focus on certain embodiments of the present invention. Such amendments have been discussed during the interview with the Examiner on May 29, 2008, and also incorporated the language "wrap" suggested by the Examiner (for which Applicants thank the Examiner). Support for the amendments may be found, for example, at page 41, lines 25-28, page 37, lines 29 and 30, page 36, lines 4-6, and page 37, lines 9 and 10 for the language "biodegradable, medicated mesh fabric wrap" and page 6, lines 19-22 for the language "the biodegradable mesh fabric wrap having coated thereon a composition that comprises a therapeutic agent and a biodegradable polymer carrier of the therapeutic agent." Claims 2, 13, 27-54, 65-72, 98, 159, 164, 189, 198,

199, and 232-235 have been amended in view of the amendments to claim 1. Claim 182 has been amended to correct a typographical error. Claim 234 has also been amended to correct improper dependency. No new matter has been added via the amendments to the claims.

Claim Rejections Under 35 U.S.C. 103(a)

Claims 1, 2, 13, 14, 21, 26, 27, 34-41, 67-69, 72 and 232 stand rejected under 35 U.S.C. 103(a) as unpatentable over Hunter *et al.* (US 5,716,981, "Hunter") in view of Cooper *et al.* (U.S. 5,962,007, "Cooper") and Datta *et al.* (US 6,338,739, "Datta").

Applicants respectfully traverse this ground of rejection. Under 35 U.S.C. 103(a), a patent claim is invalid if the differences between the claimed invention and prior art are such that the invention as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the relevant art. As reiterated by the Supreme Court in *KSR Int'l Co. v. Telefex Inc.*, 82 USPQ2d 1385 (2007), the framework for the objective analysis under 35 U.S.C. 103(a) is stated in *Graham v. John Deere Co.,* 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a legal conclusion with underlying factual consideration. *Metabolite Labs., Inc. v. Laboratory Corp. of Am. Holdings*, 370 F.3d 1354, 1368 (Fed. Cir. 2004). The factual inquiries by the Court are as follows: (1) determining the scope and content of the prior art, (2) ascertaining the differences between the claimed invention and the prior art, and (3) resolving the level of ordinary skill in the pertinent art. *Graham*, 383 U.S. at 17-18. Based on the factual inquiries, it must then be determined, whether, given the differences between the claim and the prior art, the claimed subject matter as a whole would have been obvious as a legal matter. *Nat'l Steel Car, Ltd. V. Can. Pac. Ry., Ltd.*, 357 F.3d 1319, 1334 (Fed. Cir. 2004). The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court stated that "'rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *KSR*, 82 USPQ2d at 1396.

The mere fact that the teachings of the prior art *can* be combined or modified, or that a person having ordinary skill in the art is *capable* of combining or modifying the teachings of the prior art, does not make the resultant combination *prima facie* obvious, as the prior art must also suggest the desirability of the combination (*see, e.g., In re Mills*, 16 U.S.P.Q.2d 1430, Fed. Cir. 1990; *In re Fritch*, 23 U.S.P.Q.2d 1780, Fed. Cir. 1992). In addition, "[w]hen prior art references require a selective combination to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself. Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination. It is impermissible to use the claims as a frame and the prior art references as a mosaic to piece together a facsimile of the claimed invention." *Uniroyal Inc. Rudkin-Wiley Corp.*, 837 F.2d 1044, 5 U.S.P.Q.2d 1434 (Fed. Cir. 1988).

To facilitate allowance and without acquiescing to the rejections in the Office Action, Applicants have amended claim 1 to specify the claimed subject matter to be a biodegradable, medicated mesh fabric wrap. The claimed mesh fabric wrap comprises poly(lactide-co-glycolide) with a lactide:glycolide ratio ranging from 3:97 to 15:85, and is coated with a composition that comprises a therapeutic agent and a biodegradable polymer carrier of the therapeutic agent.

Hunter, in pertinent part, relates to compositions comprising an anti-angiogenic factor and a polymeric carrier (*see*, Abstract). Anti-angiogenic factors include, for example, paclitaxel. Polymeric carriers include, for example, copolymers of lactic acid and glycolic acid, and copolymers of poly (caprolactone) or poly(lactic acid) with polyethylene glycol, and blends thereof (*see*, column 3, lines 39-61 and column 18, lines 34-36). When describing coating a stent with anti-angiogenic compositions, this reference provides that the stent may be inserted into a sleeve or mesh that is comprised of or coated with an anti-angiogenic composition (*see*, column 22, lines 50-52). In another aspect, Hunter also provides surgical meshes that have been coated with anti-angiogenic compositions (*see*, column 26, lines 19-24).

However, as to claim 1, Hunter does not mention a biodegradable mesh fabric wrap. Specifically, the "sleeve or mesh" into which a stent may be inserted according to Hunter is in an essentially tubular configuration like a stent, but not in the form of a sheet or fabric.

Hunter's disclosure of PLGA relates to polymeric carriers of anti-angiogenic factors, not as a material from which a mesh is made. Hunter does not mention a biodegradable mesh fabric wrap. In addition, Hunter also does not teach the specific range of lactide:glycolide ratio (*i.e.*, from 3:97 to 15:85). As to claim 2, it does not teach knit mesh. As to claim 13, Hunter does not specify that the poly(lactide-co-glycolide) is poly(**L**-lactide-co-glycolide). As to claims 38 and 39, Hunter does not specify the range of methoxypoly(ethylene glycol):polyester ratio (*i.e.*, about 10:90 to about 30:70) in claim 38 or the particular ratio (*i.e.*, about 20:80) in claim 39.

Cooper relates to a process for deploying a medical construct in a body cavity to function as a biodegradable stent in a body lumen. The construct is used by forming a coil from a strand that has an interior and an exterior portion, and thereafter heating while expanding the coil to melt only the exterior portion. When that melted portion resolidifies with the coil in the expanded state, the coil's integrity and resistance against forces such as compression is maintained by the unmelted but stretched interior portion, and the expanded shape is maintained by the adhesiveness of the solidified exterior portion. Such a design is intended to address problems associated with a biodegradable thermoplastic stent, especially the weakening of the strength properties of the stent when the stent is melted during its deployment. Cooper provides that regarding the materials of exterior and interior portions, most preferably, the exterior portion comprises a polyester selected from the group consisting of stiff, rigid high T_g/T_m polymers, copolymers and blends of poly(lactide) and poly(gloycolide) while the interior portion comprises a polyester selected from soft, flexible, low T_g/T_m polymers, copolymers, and blends of poly(ε-caprolactone), and copolymers and blends of poly(p-dioxanone) and poly(trimethylene carbonate) (*see*, column 4, lines 1-8). "T_g" is defined in this reference as the glass transition temperature, and T_m as the melting temperature. It further provides that "[h]ighly preferred rations of comonomers include, e.g., co-glycolide/lactide in rations of (95:5) to (5:95)" (*see*, column 4, lines 8-10). Cooper states that the interior or exterior polymers may be used as a drug delivery matrix via mixing the polymer with a therapeutic agent. However, paclitaxel is not specifically identified in a large list of drugs in Cooper. In addition, no working example in which poly(lactide-co-glycolide) was used in constructing a stent has been provided in Cooper.

Datta also relates to a biodegradable stent for implantation into a lumen in a human body. The stent is made from a biodegradable fiber having an inner core and an outer layer. The outer layer is a blend of two polymer components, such as a blend of (1) a glycolide-rich, lactide/glycolide copolymer containing at least 80 mole percent of polymerized glycolide and (2) a lactide-rich copolymer containing at least 50 mole percent of polymerized lactide (*see*, column 3, lines 49-58). The inner core is made from a biodegradable polymer made from the monomers selected from the group consisting of lactide, glycolide paradioxanone, caprolactone, and trimethylene carbonate, caprolactone blends thereof and copolymers thereof (*see*, column 3, lines 39-43). The inner core is degraded faster than the outer layer. Such a biodegradable stent is intended to be degraded into soft particles or soft fibrous elements to avoid irritation, obstruction, pain or discomfort to the patient resulting from the degradation products of the stent, after it is implanted to the patient for a prescribed, clinically appropriate period of time (*see*, column 2, line 65 to column 3, line 2). Similar to Cooper, although the polymers and polymer blends may be used as a drug delivery matrix, paclitaxel is not mentioned, nor are types of drugs with which paclitaxel shares properties (*see*, column 12, lines 8-21).

Applicants respectfully submit that one of ordinary skill in the art would not have modified Hunter in view of Cooper and Datta to arrive at the claimed subject matter of the present application. First, none of the three cited references discloses a biodegradable mesh fabric wrap. It is unclear from these three references why one skilled in the art would have modified Hunter to develop a biodegradable, medicated mesh fabric wrap.

Even assuming for argument's sake that one skilled in the art would wish to develop a biodegradable medicated mesh fabric wrap in view of Hunter, such a person would not have used a mesh that comprises poly(lactide-co-glycolide) with a lactide:glycolide ratio ranging from 3:97 to 15:85 in view of Cooper and Datta. In fact, that person would not have considered the disclosure of Cooper or Datta if he were to modify Hunter to arrive at the claimed biodegradable, medicated mesh fabric wrap of the present application. This is because Cooper and Datta both relate to biodegradable stents (intravascular devices), not biodegradable mesh fabric wraps (*e.g.*, perivascular devices), and concern with issues that are not pertinent to the development of biodegradable mesh fabric wraps (*e.g.*, perivascular devices).

More specifically, as discussed briefly above, Cooper is aimed at solving the problem of weakened strengths of biodegradable thermoplastic stents resulting from melting during their deployments. Having sufficient strength against compressive forces that tend to reclose the lumen opened by a biodegradable stent is critical for such stents. To address the above-noted issue, Cooper forms a coil from a strand that has an interior and an exterior portion and thereafter heating while expanding the coil so as to melt only the exterior portion. When that melted portion re-solidifies with the coil in the expanded state, the coil's integrity and resistance against forces (such as compression) are maintained by the un-melted but stretched interior portion, and the expanded shape is maintained by the adhesiveness of the solidified exterior portion. Although copolymers and blends of poly(lactide) and poly(glycolide) are mentioned as a preferred material for the interior portion, in selecting such a material, the glass transition and melting temperatures of those copolymers and blends of polymers are considered. Such physical features of the copolymers may not be as important a consideration for designing a mesh fabric wrap of the present application as for designing a biodegradable stent in Cooper. In addition, the broad range of lactide:glycolide ratio described in Cooper (*i.e.*, 95:5 to 5:95) provides little guidance to choose the proper lactide:glycolide ratio for selecting proper copolymers of poly(lactide) and poly(glycolide) as the material for the interior portion of a biodegradable stent in Cooper, even less guidance (if any at all) for selecting proper copolymers of lactide and glycolide as the material of a biodegradable, medicated mesh fabric wrap of the present application.

Datta is aimed at minimizing the problems resulting from degradation products of biodegradable stents, such as irritation, obstruction, pain or discomfort to the patients in which the stents are implanted while withstanding radial stresses to perform their function of maintaining an open passage through a lumen. According to Datta, although prior art biodegradable stents, such as those made from a high-lactide polymer, provide excellent initial mechanical properties and excellent retention of those properties with time, when they start to degrade, they usually fail by way of a catastrophic failure mechanism (see, column 11, lines 19-27). Datta further states that "[u]tilizing copolymerization of lactide and glycolide (whether in a random, segmented or block nature-ranging from polyglycolide homopolymer to polylactide

homopolymer), a combination of properties, such as suitable initial mechanical properties, suitable excellent retention of those properties with time, and softening failure mechanism, is very difficult if not impossible to achieve" (*see*, column 11, lines 42-47). To achieve softening failure mechanism, the stent of Datta has an outer layer made from a blend of two polymer components: one faster degrading polymer and one slower degrading polymer. For example, one polymer is a glycolide-rich, lactide/glycolide copolymer containing at least 80 mole percent of polymerized glycolide, and the other is a lactide-rich copolymer containing at least 50 mole percent of polymerized lactide. Thus, the concerns and considerations in developing biodegradable stents in Datta are different from those in developing a biodegradable, medicated mesh fabric wrap, such as a biodegradable, medicated perivascular wrap, in the present application. For example, obstruction of a blood vessel resulting from the degradation products of a delivery device and maintaining resistance against radical compression are of concern when developing a biodegradable stent, not when developing a mesh fabric wrap (*e.g.*, a perivascular wrap). In addition, to the extent that a softening failure mechanism may be desirable for a mesh fabric wrap (*e.g.*, a perivascular wrap), such as to minimize irritation, pain or discomfort to a patient, Datta teaches the use of a blend of copolymers, and teaches away from the use of a single copolymer, poly(lactide-co-glycolide). Thus, one of ordinary skill in the art, in view of Datta, would not be motivated to use a material other than a blend of copolymers, such as the copolymer recited in claim 1 of the present application (*i.e.*, poly(lactide-co-glycolide) with a lactide:glycolide ratio ranging from 3:97 to 15:85) to make a mesh fabric wrap (*e.g.*, a perivascular wrap).

In summary, Applicants submit that claim 1 is not obvious over Hunter in view of Cooper and Datta because one of ordinary skill in the art would not have modified Hunter in view of Cooper and Datta to arrive at the claimed subject matter of the present application. Specifically, such a person would not have considered developing a biodegradable, medicated mesh fabric wrap (*e.g.*, a perivascular wrap) in view of the cited references because none of them discloses a biodegradable mesh fabric wrap. In addition, that person would not have considered Cooper and Datta because they relate to biodegradable stents and deal with problems different from those of developing mesh fabric wraps (*e.g.*, perivascular wraps). Even assuming for

argument's sake that a person would combine the teachings of Cooper and Datta with Hunter, he or she would not have arrived at the subject matter claimed in the present application because neither of these two cited references provides sufficient guidance to modify Hunter to use a biodegradable mesh fabric wrap that comprises poly(lactide-co-glycolide) with a lactide:glycolide ratio ranging from 3:97 to 15:85 to make a biodegradable, medicated mesh fabric wrap.

As to claim 2, in addition to the above arguments against the obviousness rejection against claim 1, Applicants further disagree with the statement in the Office Action that "since a mesh can either be woven, non-woven or knitted (sic), it would be obvious to have the mesh woven or non-woven or knit so that claim 2 is met." Because no reasons for, or advantages of, using a knit mesh are disclosed in Hunter, Cooper or Datta or otherwise, should this rejection be maintained, Applicants respectfully request that such reasons or advantages be provided.

As to claims 38 and 39, in addition to the above arguments against the obviousness rejection against claim 1, Applicants further submit that the cited references, either alone or in combination, fail to teach or suggest the specific methoxypoly(ethylene glycol):polyester ratio range recited in claim 38 or the specific methoxypoly(ethylene glycol):polyester ratio recited in claim 39.

In view of the above remarks, Applicants submit that this ground of rejection under 35 U.S.C. 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

Claims 1, 26 and 34-41 stand rejected under 35 U.S.C. 103(a) as unpatentable over Hunter *et al.* (US 5,716,981, "Hunter") in view of Cooper *et al.* (U.S. 5,962,007, "Cooper") and Datta *et al.* (US 6,338,739, "Datta") and further in view of Zhang *et al.* (International Journal of Pharmaceutics 132: 195-206, 1996, "Zhang"). It is asserted in the Office Action that "Zhang teaches that the molecular weight of the MePEG and the weight ratio of the PDLLA and MePEG influence the ability of the polymer in solubilizing taxol." It is concluded in the Office Action that "one having ordinary skill in the art at the time the invention was made would have [a] reasonable expectation of success that taking the teachings of the references together,

modification of the polymer in view of the teachings of Zhang would lead to [a] composition that would give the desired solubility of paclitaxel, which is a taxol."

Applicants respectfully traverse this ground of rejection. As discussed above, claims 1, 26 and 34-41 are not obvious over Hunter in view of Cooper and Datta. Briefly, none of Hunter, Cooper and Datta discloses a biodegradable mesh fabric wrap (*e.g.*, a biodegradable perivascular wrap). In addition, one of ordinary skill in the art would not have considered Cooper and Datta to develop a biodegradable, medicated mesh fabric wrap (*e.g.*, a biodegradable, medicated perivascular wrap) because these two references relate to biodegradable stents and deal with problems different from those of developing mesh fabric wrap (*e.g.*, perivascular wraps). Even assuming for argument's sake that one would combine the teachings of Cooper and Datta with Hunter, that person would not have arrived at the subject matter claimed in the present application because neither of the cited references provides sufficient guidance to modify Hunter so that a mesh fabric wrap that comprises poly(lactide-co-glycolide) with a lactide:glycolide ratio ranging from 3:97 to 15:85 is used to provide a biodegradable, medicated mesh fabric wrap.

The above deficiencies of Hunter, Cooper and Datta as the basis of an obviousness rejection against claim 1 of the present application has not been remedied by Zhang. More specifically, Zhang relates to development of diblock PDLLA-MePEG copolymers as a micellar carrier of taxol. It is silent with respect to mesh fabric wraps and PLGA as mesh materials. Accordingly, adding Zhang as another reference would not have rendered claim 1 obvious.

Applicants further submit that one of ordinary skill in the art would not have been motivated by Zhang to modify Hunter to arrive at the claimed subject matter of claims 34-41 of the present invention with a reasonable expectation of success. Zhang describes the use of diblock PDLLA-MePEG copolymers as a micellar carrier of taxol. Differences between the micellar compositions according to Zhang and the compositions as part of a mesh fabric wrap (*e.g.*, a perivascular wrap) according to the present application limit the relevance or applicability of using diblock PDLLA-MePEG as a carrier of paclitaxel for developing a paclitaxel-containing mesh fabric wrap (*e.g.*, a paclitaxel-containing perivascular wrap). For example, one skilled in

the art would appreciate that the release profile of paclitaxel from a micellar composition is likely to be different from that from a coating of a mesh fabric wrap (*e.g.*, a perivascular wrap) after being implanted into a patient. Accordingly, it is unlikely that one of ordinary skill in the art would have chosen PDLLA-MePEG as the carrier of paclitaxel in developing a paclitaxel-containing mesh fabric wrap (*e.g.*, a paclitaxel-containing perivascular wrap) in view of Zhang as a whole. Even assuming for argument's sake that such a person had chosen PDLLA-MePEG as the carrier of paclitaxel, there would not have been a reasonable expectation of success that the resulting biodegradable, medicated mesh fabric wrap (*e.g.*, a biodegradable, medicated perivascular wrap) would have desirable properties for sustained release of paclitaxel from the mesh fabric wrap.

In view of the above remarks, Applicants submit that this ground of rejection under 35 U.S.C. 103(a) has been overcome. Withdrawal of these rejections is respectfully requested.

Claims 1 and 232 stand rejected under 35 U.S.C. 103(a) as unpatentable over Hunter *et al.* (US 5,716,981, "Hunter") in view of Cooper *et al.* (U.S. 5,962,007, "Cooper") and Datta *et al.* (US 6,338,739, "Datta") and further in view of Schrayer (US 6,575,887, "Schrayer"). It is stated in the Office Action that one of the goals of Hunter is the embolization of blood vessels in the treatment of tumors using a paclitaxel-containing composition. It is further stated in the Office Action that Schrayer teaches wrapping blood vessels to mitigate overexuberant cellular proliferation. It is thus concluded in the Office Action that "one having ordinary skill in the art [at] the time the invention was made would have [a] reasonable expectation of success that wrapping the blood vessels in diseased tumor or cancer conditions would successfully mitigate proliferating cellular conditions."

Applicants respectfully traverse this ground of rejection. As discussed above, claim 1 is not obvious over Hunter in view of Cooper and Datta because (1) none of Hunter, Cooper and Datta discloses a biodegradable mesh fabric wrap (*e.g.*, a perivascular wrap), (2) Cooper and Datta both relate to biodegradable stents and deal with problems different from those of developing mesh fabric wraps, and (3) neither Cooper nor Datta provides sufficient guidance

to modify Hunter so that a mesh fabric wrap that comprises poly(lactide-co-glycolide) with a lactide:glycolide ratio ranging from 3:97 to 15:85 is used to develop a biodegradable, medicated mesh fabric wrap.

The above-noted last deficiency of Hunter, Cooper and Datta as the basis of an obviousness rejection against claim 1 of the present application has not been remedied by Schrayer. More specifically, Schrayer relates to a surgically implantable radioactive wrap that may be positioned around the wall of a blood vessel to maintain patency of the blood vessel wall by mitigating overexuberant cellular proliferation. It is silent with respect to the use of a mesh fabric wrap that comprises poly(lactide-co-glycolide) with a lactide:glycolide ratio ranging from 3:97 to 15:85 in developing a medicated mesh fabric wrap.

In addition, Applicants submit that there would not have been a reasonable expectation of success in modifying Hunter in view of Schrayer to develop a paclitaxel-containing mesh fabric wrap (*e.g.*, a paclitaxel-containing perivascular wrap). More specifically, as indicated above, Schrayer relates to a surgically implantable radioactive wrap that may be used to mitigate overexuberant cellular proliferation. One skilled in the art would appreciate that delivery of radiation across a blood vessel wall is different from delivery of a drug, such as paclitaxel. For example, the ability of radiation to penetrate through a blood vessel wall is different from that of paclitaxel. In addition, mechanisms useful for limiting exposure of radiation to healthy tissue or cells (*e.g.*, a radiation shield element or a radiation attenuation element) are typically not applicable to minimizing unintended delivery or diffusion of paclitaxel to healthy tissue or cells. Accordingly, success in using a radioactive wrap in mitigating overexuberant cellular proliferation does not provide a reasonable expectation of success in using paclitaxel-containing mesh fabric wrap (*e.g.*, a perivascular wrap) in treating similar conditions.

In view of the above remarks, Applicants submit that this ground of rejection under 35 U.S.C. 103(a) has been overcome. Withdrawal of these rejections is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants believe that all of the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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